Containing the Hong Kong Poultry Flu

n May 21, 1997, a 3-yearold boy in Hong Kong died of medical complications from a flu virus, and suddenly the world held its breath.

Hong Kong and other locations in

China have a history of being the starting zones for world influenza pandemics worldwide epidemics bringing illness and death to millions of people. In 1957, and again in 1968, new flu pandemics arose from this part of Asia. Would Hong Kong be the beginning of another one like the Spanish flu, the worst influenza of the 20th century, which killed 30 million people from 1918 to 1919?

ries at the National Institute for Medical Research in London, England, and the National Influenza Center at Rotterdam, The Netherlands.

Atlanta, August 1: At the CDC, microbiologist Nancy Cox faces two

OUTBREAK

To test its effect, veterinarian David Swayne will inoculate chickens with virus extracted from this breeder stock vial.

What happened in the months that followed the young boy's death is a story of quick thinking and teamwork between private and public research agencies, including USDA's Agricultural Research Service. This time, no pandemic occurred. But scientists got an important drill in prevention, and the world got a wake-up call.

Hong Kong, May 21: The 3-year old victim's physician sends samples of respiratory secretions from the child to the Hong Kong Department of Health. In a laboratory there, an unusual influenza virus is obtained from this clinical sample. Department of Health officials forward this virus to the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and to counterpart laborato-

big tasks—a scientific one and a practical one. She has just learned that the European labs, working independently, reached the same conclusion as the CDC: The mystery virus is H5N1, short for hemagglutinin subtype 5 and neuraminidase subtype 1, both proteins on the virus surface.

But H5N1 is a bird virus. Has it changed hosts? More important, can the infection pass from birds to humans? Or, even worse, has the virus developed a deadly new trick: the ability to pass from person to person? This is how pandemics start.

One way to answer the scientific questions, Cox knows, is to compare viral genes from the boy's sample with virus from an infected chicken. But handling such viruses requires a special lab—a biosafety level-3 (BSL-3)—designed to contain deadly viruses. CDC Influenza Branch does not have a BSL-3 laboratory available for use: Human influenza viruses are handled in a lower level of bio-

containment, BSL-2.

Atlanta, August 25: Cox reaches for the phone and dials David E. Swayne. In Athens, about an hour east of Atlanta, Swayne, a veterinarian, heads the ARS Southeast Poultry Research Laboratory (SEPRL). He leads a team of experts studying poultry influenza viruses, including the H5 subtype. In 1994 and 1995. the Athens re-

searchers helped understand an outbreak in Mexico of H5N2, a poultry virus strain not seen in humans.

Swayne and colleague Mike Perdue, a microbiologist, have been working with several companies to come up with poultry vaccines for H5-type viruses. Their laboratory has both a BSL-3 facility and sophisticated means of detecting and identifying these viruses. This gives them the ability to work without endangering humans or poultry in the surrounding community.

Swayne agrees to help, recognizing the importance of H5N1 not only to humans, but to the U.S. poultry industry. He offers Cox's group his biocontainment facility until a CDC facility can be made available.

"The offer was immediately accepted by the CDC," says Cox.
"Having the facility was essential to analyzing the first virus from the outbreak."

The CDC experts begin an ongoing collaboration with an ARS team that includes Swayne, Perdue, veterinarian David Suarez, and microbiologist Stacey Schultz-Cherry.

Athens, end of August to early September: At the CDC's recommendation, everyone on the project begins taking rimantadine, an antiviral drug. In the containment rooms, scientists wear special masks covering nose and mouth. Later, CDC, ARS, and USDA's Animal and Plant Health Inspection Service (APHIS) upgrade their protection while working with infected poultry to include wearing air-filtering hoods that cover

Department, requests test materials for H5N1. At the time, Sims' staff is using deadly Hong Kong H5N1 virus to make diagnostic proteins, or antigens, used to detect antibodies in blood of infected birds.

While a "hot" virus makes an effective antigen, using a related, mild strain that doesn't strike humans would be safer. Swayne dispatches a courier with safer diagnostic materials from his lab to help Sims protect his employees and speed detection.

Swayne also gets a call from Charlie Beard, retired SEPL director and now vice president for research and technology for the U.S. Poultry and Egg Association, a key poultry industry trade group. Beard is concerned about protecting U.S. poultry from H5N1. Swayne briefs him on the latest findings from CDC and ARS.

90 to 100 percent effective if the right dosage and protocols are used. In a majority of the 20-bird test flocks, the virus that could kill in 24 hours is now defeated.

Hong Kong, December 29:

While vaccine may have been found, Hong Kong officials aren't taking chances. They begin a mass slaughter of 1.5 million chickens and an industrywide cleanup of poultry markets.

Athens, December 30: Beard calls Swayne, concerned about whether a protocol for poultry vaccination should be developed, considering how lethal H5N1 is to birds. Swayne reassures him one is under way. This is important, as accidental infections could endanger the world's valuable poultry breeding stock and ultimately contribute to shortages of poultry meat and eggs.

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the head and protect the eyes.

Suarez and Perdue sequence the genetic material of the chicken viruses from Hong Kong and, with CDC, compare this information to the H5N1 viruses from people. This shows that the human viruses were from birds.

Swayne discovers that the human virus kills test poultry in less than 48 hours. The virus replicates in vascular endothelial cells—those that line blood vessels throughout the body—and in muscle cells of the heart. The H5N1 virus from chickens attacks poultry the same way as this human-source virus. Schultz-Cherry shows a host protein that may be a factor in the disease.

Hong Kong, December 2: In a fax to Swayne, Les Sims, with Hong Kong's Agriculture and Fisheries

Hong Kong, December 5: H5N1 claims the life of a 54-year-old man in Hong Kong.

Athens, December 17: Swayne begins a new test of H5N1's virulence. Using virus isolated from a blood sample of the latest victim, he infects a poultry flock of about 20 birds in the Athens biocontainment facility. Within 24 hours, the entire flock is dead.

"It wasn't the fact that they died that struck me," he recalls. "It was how quickly it happened."

This finding heightens a previously raised question: Should there be an emergency protocol for vaccinating U.S. poultry? Swayne, Perdue, and Suarez decide to test three vaccines developed for other H5 poultry influenza viruses. All are

Washington, D.C., January 8, 1998: Swayne and Beard meet with

APHIS leaders, who decide to approve the industry's stockpiling of H5 vaccines, in the event the virus spreads outside of Hong Kong. APHIS drafts an emergency vaccination plan.

Washington, D.C. January 18:

A joint CDC-ARS article appears in *Science* describing the characteristics of the first human H5N1 virus from Hong Kong.

Hong Kong, late March: No new cases of H5N1 have been reported for some time. Swayne and Perdue fly to Hong Kong with new poultry vaccines they co-developed with several cooperators. They provide Les Sims samples, so he can test them at the Hong Kong Agriculture and Fisheries Department. Perdue visits zoo offi-

Yeast May Inhibit Salmonella

cials and helps test the vaccine in some exotic birds.

Washington, D.C., August, 1998: A joint ARS-CDC article appears in the *Journal of Virology* fully describing the first human and poultry strains.

At Present: Though the origin of H5N1 is still unknown, the massive worldwide media coverage has died down as the outbreak has subsided. The virus fades into "old news."

The Hong Kong government, initially criticized for destroying all its poultry to eradicate potential virus

ROB FLYNN (K8254-13)

Veterinary medical officers David Suarez (left) and David Swayne evaluate tissue sections (top monitor) from chickens infected with Hong King H5N1 influenza. The bottom monitor displays a photo of chicken legs showing physical damage resulting from the flu virus.

carriers, is now credited with preventing a more serious outbreak.

Research teams worldwide, including those led by Sims, Cox, and Swayne, continue to study H5N1 to find out what enabled it to change hosts. If they can discover why this happened, they may be able to stop similar outbreaks sooner.—By Jill Lee, ARS.

David E. Swayne, USDA-ARS Southeast Poultry Research Laboratory, 934 College Station Rd., Athens, GA 30605; phone (706) 546-3433, fax (706) 546-3161, e-mail dswayne@arches.uga.edu. ◆ Yeast is good for beer and bread—and it might even be good for chickens or turkeys. That's because a special yeast, *Saccharomyces boulardii*, may help make poultry foods even safer for people to eat.

It's no secret that *Campylobacter* and *Salmonella* are the main foodborne pathogens likely to contaminate live poultry. A special problem: These pathogens skyrocket when birds are off feed and in the transport trucks going to slaughter. That means the birds often arrive at the processing plant with higher bacterial counts than when they left the farm.

Food technologist J. Eric Line, who is in the ARS Poultry Microbiological Safety Research Unit at Athens, Georgia, found that feeding chickens the *S. boulardii* yeast a couple of days before transport helped. He exposed flocks of poultry to various strains of *Salmonella* and *Campylobacter*, then put them through a simulated transport.

Salmonella counts increased about fivefold in untreated control birds during transport. Chickens given the yeast had no increase in *Salmonella*.

Results from a second experiment showed untreated birds increased their *Salmonella* loads from 53 to 67 percent during transport. With yeast, the birds' *Salmonella* levels decreased 40 percent. While some *Campylobacter* levels did go down, the treatment was not as effective for this pathogen.

Overall, the *S. boulardii* yeast's food safety benefits could be important for farmers and plant managers alike, since federal law requires them to identify key contamination points and take steps to reduce risk—including during transport.

"This yeast is generally recognized as safe for people and animals," says Line. "We're pleased that results show the reduction of *Salmonella*, because that's something American consumers want—poultry that is *Salmonella*-free from farm to table."

Line adds that there is still much research to be done on this treatment. First, farmers won't use it, he says, unless they can do so economically. That means refining the treatment with farmers' operating budgets in mind.

But the treatment—for which Line has filed a patent—would be one part of a complete food safety protocol. He cautioned that no single thing will work as a "magic bullet" to reduce *Salmonella* in poultry.—By **Jill Lee,** ARS.

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